```
Connecting via Winsock to STN


Welcome to STN International!  Enter x:x

LOGINID:SSPTAEXO1623

PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'BIOSIS, EMBASE, MEDLINE' AT 16:29:03 ON 23 OCT 2006
FILE 'BIOSIS' ENTERED AT 16:29:03 ON 23 OCT 2006
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FILE 'EMBASE' ENTERED AT 16:29:03 ON 23 OCT 2006
Copyright (c) 2006 Elsevier B.V. All rights reserved.
FILE 'MEDLINE' ENTERED AT 16:29:03 ON 23 OCT 2006f

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      23.48      25.52

=> file registry
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      23.48      25.52

FILE 'REGISTRY' ENTERED AT 16:29:09 ON 23 OCT 2006
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STRUCTURE FILE UPDATES:   22 OCT 2006  HIGHEST RN 911002-75-0
DICTIONARY FILE UPDATES:  22 OCT 2006  HIGHEST RN 911002-75-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

  Please note that search-term pricing does apply when
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REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> s clitocine/cn
L8            1 CLITOCINE/CN

=> d l8

L8   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   105798-74-1  REGISTRY
ED   Entered STN:  21 Dec 1986
CN   β-D-Ribofuranosylamine, N-(6-amino-5-nitro-4-pyrimidinyl)- (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   Clitocine
```
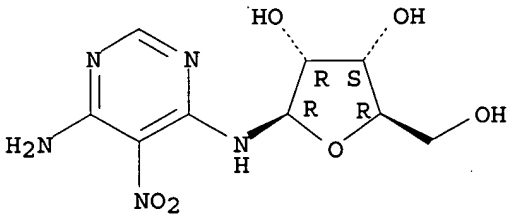

FS STEREOSEARCH
MF C9 H13 N5 O6
CI COM
SR CA
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, DDFU, DRUGU, IPA, MEDLINE, NAPRALERT, PROUSDDR, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

19 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
19 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.10	32.62

FILE 'CAPLUS' ENTERED AT 16:29:35 ON 23 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 23 Oct 2006 VOL 145 ISS 18
FILE LAST UPDATED: 22 Oct 2006 (20061022/ED)

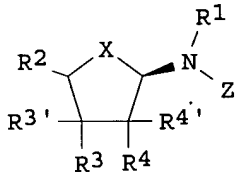
Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

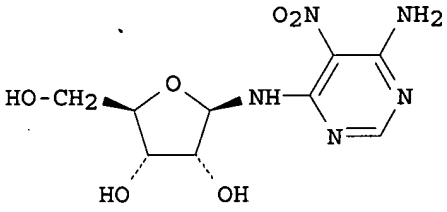
=> s l8
L9 19 L8

=> s l9 and ((muscular(w)dystrophy) or (cystic(w)fibrosis) or (nonsense(w)suppres?) or (premature(w)stop(w)codon))
25752 MUSCULAR
12657 DYSTROPHY
8644 MUSCULAR(W)DYSTROPHY

```
         15664 CYSTIC
         34783 FIBROSIS
         11864 CYSTIC(W)FIBROSIS
          7918 NONSENSE
        400106 SUPPRES?
           448 NONSENSE(W)SUPPRES?
         30766 PREMATURE
         39587 STOP
         37627 CODON
           938 PREMATURE(W)STOP(W)CODON
L10         2 L9 AND ((MUSCULAR(W)DYSTROPHY) OR (CYSTIC(W)FIBROSIS) OR (NONSE
              NSE(W)SUPPRES?) OR (PREMATURE(W)STOP(W)CODON))

=> d l10 1-2 ti abs bib

L10  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Preparation of nucleoside analogs for treating or preventing diseases
     associated with nonsense mutations of mRNA
GI
```



I



II

AB Nucleoside analogs I, wherein Z is (un)substituted alkyl, (un)substituted (un)substituted aryl, (un)substituted heteroaryl, (un)substituted cycloalkyl, (un)substituted heterocycle; X is CH, O, S, NH; R1 is H, (un)substituted alkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted cycloalkyl, (un)substituted heterocycle; R2 is (un)substituted alkyl, carboxy, amido, acyl, alkylcarbonyl, halogen, azide, alkyl amino, phosphate, phosphoester, alkyl ether; R3, R3', R4, R4' are independently (un)substituted ether, H, halogen, (un)substituted alkyl, (un)substituted (un)substituted aryl, (un)substituted heteroaryl, (un)substituted cycloalkyl, (un)substituted heterocycle are prepared for use in the treatment or prevention of diseases associated with nonsense mutations of mRNA. Thus, II was prepared and tested in a cell-based luciferase reporter assay containing a UGA premature termination codon that was stably transfected in 293T Human Embryonic Kidney cells (no data but very high potency and very high efficacy of protein synthesis). Further, I can be used as a prodrug in the treatment of autoimmune disease, blood diseases, collagen diseases, diabetes, neurodegenerative diseases, cardiovascular diseases, pulmonary diseases, inflammatory diseases, central nervous system diseases.

AN 2006:740594 CAPLUS
DN 145:167496
TI Preparation of nucleoside analogs for treating or preventing diseases associated with nonsense mutations of mRNA
IN Wilde, Richard G.; Almstead, Neil G.; Welch, Ellen M.; Beckmann, Holger
PA USA

SO U.S. Pat. Appl. Publ., 47 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006166926	A1	20060727	US 2005-48659	20050121
PRAI US 2005-48659		20050121		

OS MARPAT 145:167496

L10 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
TI Use of nucleoside compounds for nonsense suppression and the treatment of genetic diseases
AB The invention encompasses nucleoside compds., compns. comprising the compds. and methods for treating or preventing diseases associated with nonsense mutations of mRNA by administering these compds. or compns. Diseases that can be treated or prevented by compds. of the invention include, but are not limited to, cancer, autoimmune diseases, blood diseases, collagen diseases, diabetes, neurodegenerative diseases, cardiovascular diseases, pulmonary diseases, inflammatory diseases, lysosomal storage disease, tuberous sclerosis or central nervous system diseases. The present invention is based in part on the discovery of small mols. that modulate premature translation termination and/or nonsense-mediated mRNA decay.
AN 2004:80704 CAPLUS
DN 140:122839
TI Use of nucleoside compounds for nonsense suppression and the treatment of genetic diseases
IN Wilde, Richard G.; Almstead, Neil G.; Welch, Ellen M.; Beckmann, Holger
PA PTC Therapeutics, Inc., USA; Tularik Inc.
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004009610	A2	20040129	WO 2003-US23185	20030723
WO 2004009610	A3	20051006		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2493816	AA	20040129	CA 2003-2493816	20030723
AU 2003261237	A1	20040209	AU 2003-261237	20030723
EP 1572709	A2	20050914	EP 2003-766015	20030723
EP 1572709	A3	20051123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI US 2002-398334P	P	20020724		
WO 2003-US23185	W	20030723		

OS MARPAT 140:122839

=> s l9 and (readthrough)
986 READTHROUGH
L11 1 L9 AND (READTHROUGH)

```
=> d l11 ti

L11  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Use of nucleoside compounds for nonsense suppression and the treatment of
     genetic diseases


=> file uspatfull
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        27.15      59.77

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                        -1.50      -1.50

FILE 'USPATFULL' ENTERED AT 16:31:54 ON 23 OCT 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 19 Oct 2006 (20061019/PD)
FILE LAST UPDATED: 19 Oct 2006 (20061019/ED)
HIGHEST GRANTED PATENT NUMBER: US7124445
HIGHEST APPLICATION PUBLICATION NUMBER: US2006236437
CA INDEXING IS CURRENT THROUGH 19 Oct 2006 (20061019/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 19 Oct 2006 (20061019/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006


=> s l8
L12           2 L8

=> s l12 and ((muscular(w)dystrophy) or (cystic(w)fibrosis) or
(nonsense(w)suppres?) or (premature(w)stop(w)codon))
         26657 MUSCULAR
          8176 DYSTROPHY
          5446 MUSCULAR(W)DYSTROPHY
         15149 CYSTIC
         24672 FIBROSIS
         12495 CYSTIC(W)FIBROSIS
          4379 NONSENSE
        365999 SUPPRES?
           112 NONSENSE(W)SUPPRES?
         88242 PREMATURE
        670811 STOP
         53519 CODON
           627 PREMATURE(W)STOP(W)CODON
L13           2 L12 AND ((MUSCULAR(W)DYSTROPHY) OR (CYSTIC(W)FIBROSIS) OR (NONSE
                NSE(W)SUPPRES?) OR (PREMATURE(W)STOP(W)CODON))

=> d l13 1-2 ti

L13  ANSWER 1 OF 2  USPATFULL on STN
TI     Use of nucleoside compounds for nonsense suppression
       and the treatment of genetic diseases

L13  ANSWER 2 OF 2  USPATFULL on STN
TI     Nucleoside compounds and their use for treating cancer and diseases
       associated with somatic mutations


=> d l13 2 ti abs bib

L13  ANSWER 2 OF 2  USPATFULL on STN
TI     Nucleoside compounds and their use for treating cancer and diseases
```

```
       associated with somatic mutations
AB     The invention encompasses nucleoside compounds, compositions comprising
       the compounds and methods for treating or preventing diseases associated
       with nonsense mutations of mRNA by administering these compounds or
       compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN     2004:88924  USPATFULL
TI     Nucleoside compounds and their use for treating cancer and diseases
       associated with somatic mutations
IN     Wilde, Richard G., Somerville, NJ, UNITED STATES
       Kennedy, Paul D., Kalamazoo, MI, UNITED STATES
       Almstead, Neil G., Holmdel, NJ, UNITED STATES
       Welch, Ellen M., Califon, NJ, UNITED STATES
       Takasugi, James J., Lawrenceville, NJ, UNITED STATES
       Friesen, Westley J., Huntingdon Valley, PA, UNITED STATES
PI     US 2004067900      A1   20040408
AI     US 2003-625059     A1   20030722 (10)
PRAI   US 2002-398334P     20020724 (60)
DT     Utility
FS     APPLICATION
LREP   JONES DAY, 222 EAST 41ST STREET, NEW YORK, NY, 10017
CLMN   Number of Claims: 28
ECL    Exemplary Claim: 1
DRWN   4 Drawing Page(s)
LN.CNT 3696
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               4.88      64.65

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                               0.00      -1.50

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
       AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
       CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
       DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 16:32:58 ON 23 OCT 2006

68 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s clitocine and ((nonsense(w)suppres?)or(readthrough) or(premature(w)stop))
  26 FILES SEARCHED...
           1   FILE IFIPAT
           1   FILE PROUSDDR
  56 FILES SEARCHED...
           2   FILE USPATFULL

   3 FILES HAVE ONE OR MORE ANSWERS,   68 FILES SEARCHED IN STNINDEX

L14  QUE CLITOCINE AND ((NONSENSE(W) SUPPRES?) OR(READTHROUGH) OR(PREMATURE(W)
         STOP))

=> d hid
DISPLAY L# IS NOT VALID IN STNINDEX
Answer set was created in a file.  Enter DISPLAY HISTORY to see where
the answer set was created.  Use the File command to change to that
```

```
file, then display the answer.

=> d hid
DISPLAY L# IS NOT VALID IN STNINDEX
Answer set was created in a file.  Enter DISPLAY HISTORY to see where
the answer set was created.  Use the File command to change to that
file, then display the answer.

=> d his

     (FILE 'HOME' ENTERED AT 15:10:21 ON 23 OCT 2006)

     INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
     AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
     CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
     DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 15:10:36 ON 23 OCT 2006
               SEA FORSKOLIN AND (POTASSIUM(W)CHANNEL)
               ---------
                 2   FILE AGRICOLA
                 1   FILE AQUASCI
                 1   FILE BIOENG
               244   FILE BIOSIS
                 4   FILE BIOTECHABS
                 4   FILE BIOTECHDS
                79   FILE BIOTECHNO
                 3   FILE CABA
               402   FILE CAPLUS
                24   FILE DDFU
                 5   FILE DISSABS
                38   FILE DRUGU
                 1   FILE EMBAL
               505   FILE EMBASE
                48   FILE ESBIOBASE
                35   FILE IFIPAT
                 1   FILE IMSRESEARCH
                16   FILE JICST-EPLUS
                14   FILE LIFESCI
               189   FILE MEDLINE
                21   FILE PASCAL
               121   FILE SCISEARCH
               151   FILE TOXCENTER
               247   FILE USPATFULL
                30   FILE USPAT2
                 1   FILE VETU
                14   FILE WPIDS
                14   FILE WPINDEX
L1               QUE FORSKOLIN AND (POTASSIUM(W) CHANNEL)
                 ---------

     FILE 'BIOSIS, EMBASE, MEDLINE' ENTERED AT 15:12:06 ON 23 OCT 2006
L2           938 S FORSKOLIN AND (POTASSIUM(W)CHANNEL)
L3           182 S L2 AND (ATP(W)(SENSITIVE OR ACTIVATED))
L4           154 S L3 NOT PY>2003
L5           104 DUP REM L4 (50 DUPLICATES REMOVED)
L6            19 S L5 AND (ADENYLYL(W)CYCLASE)
L7             0 S L5 AND (BLOOD-BRAIN)

     FILE 'REGISTRY' ENTERED AT 16:29:09 ON 23 OCT 2006
L8             1 S CLITOCINE/CN

     FILE 'CAPLUS' ENTERED AT 16:29:35 ON 23 OCT 2006
L9            19 S L8
L10            2 S L9 AND ((MUSCULAR(W)DYSTROPHY) OR (CYSTIC(W)FIBROSIS) OR (NO
L11            1 S L9 AND (READTHROUGH)
```

```
     FILE 'USPATFULL' ENTERED AT 16:31:54 ON 23 OCT 2006
L12             2 S L8
L13             2 S L12 AND ((MUSCULAR(W)DYSTROPHY) OR (CYSTIC(W)FIBROSIS) OR (NO

     INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
     AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
     CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
     DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 16:32:58 ON 23 OCT 2006
                SEA CLITOCINE AND ((NONSENSE(W)SUPPRES?)OR(READTHROUGH) OR(PREM
                ---------
                1    FILE IFIPAT
                1    FILE PROUSDDR
                2    FILE USPATFULL
L14             QUE CLITOCINE AND ((NONSENSE(W) SUPPRES?) OR(READTHROUGH) OR(PR
                ---------

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     2.44      67.09

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -1.50

STN INTERNATIONAL LOGOFF AT 16:35:14 ON 23 OCT 2006
```

```
Connecting via Winsock to STN


Welcome to STN International!  Enter x:x

LOGINID:SSPTAEXO1623

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  AUG 09  INSPEC enhanced with 1898-1968 archive
 NEWS  4  AUG 28  ADISCTI Reloaded and Enhanced
 NEWS  5  AUG 30  CA(SM)/CAplus(SM) Austrian patent law changes
 NEWS  6  SEP 11  CA/CAplus enhanced with more pre-1907 records
 NEWS  7  SEP 21  CA/CAplus fields enhanced with simultaneous left and right
                  truncation
 NEWS  8  SEP 25  CA(SM)/CAplus(SM) display of CA Lexicon enhanced
 NEWS  9  SEP 25  CAS REGISTRY(SM) no longer includes Concord 3D coordinates
 NEWS 10  SEP 25  CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
 NEWS 11  SEP 28  CEABA-VTB classification code fields reloaded with new
                  classification scheme
 NEWS 12  OCT 19  LOGOFF HOLD duration extended to 120 minutes
 NEWS 13  OCT 19  E-mail format enhanced
 NEWS 14  OCT 23  Option to turn off MARPAT highlighting enhancements available
 NEWS 15  OCT 23  CAS Registry Number crossover limit increased to 300,000 in
                  multiple databases
 NEWS 16  OCT 23  The Derwent World Patents Index suite of databases on STN
                  has been enhanced and reloaded

 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8
 NEWS X25      X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that
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  result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:42:54 ON 23 OCT 2006

=> file registry
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 16:43:05 ON 23 OCT 2006
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 22 OCT 2006 HIGHEST RN 911002-75-0
DICTIONARY FILE UPDATES: 22 OCT 2006 HIGHEST RN 911002-75-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

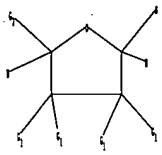
TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

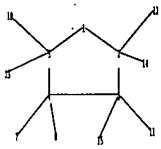
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\11048659generic.str





chain nodes :
7 8 10 11 12 13 14 15
ring nodes :
1 2 3 4 5
chain bonds :
2-12 2-14 3-11 3-15 4-7 4-8 5-10 5-13
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 2-3 2-12 3-4 3-11 3-15 4-5 4-7 4-8 5-10
exact bonds :
2-14 5-13

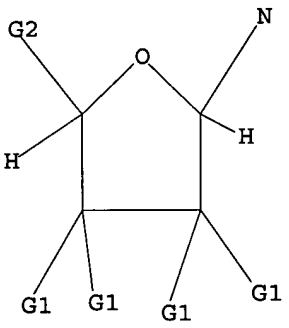
G1:C,H,O

G2:C,O

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 7:CLASS 8:CLASS 10:CLASS 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 C,H,O

G2 C,O

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam
SAMPLE SEARCH INITIATED 16:43:34 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 13585 TO ITERATE

14.7% PROCESSED 2000 ITERATIONS 18 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

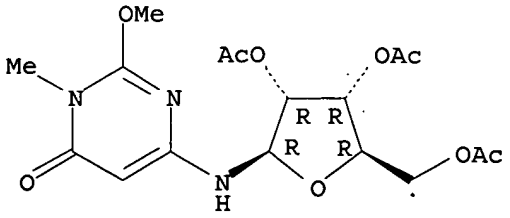
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 264718 TO 278682
PROJECTED ANSWERS: 1782 TO 3108

L2 18 SEA SSS SAM L1

=> d l2 scan

L2 18 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 4(3H)-Pyrimidinone, 2-methoxy-3-methyl-6-[(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)amino]- (9CI)
MF C17 H23 N3 O9

Absolute stereochemistry. Rotation (-).

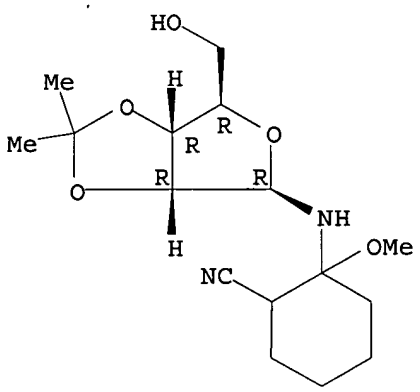


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):4

L2 18 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Cyclohexanecarbonitrile, 2-methoxy-2-[[2,3-O-(1-methylethylidene)-β-D-ribofuranosyl]amino]- (9CI)
MF C16 H26 N2 O5

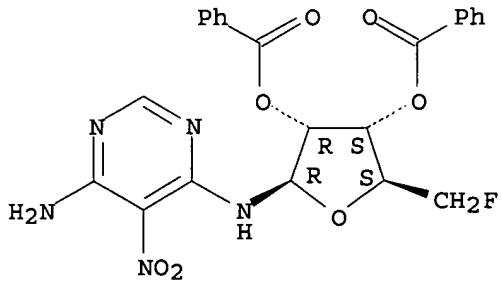
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 18 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN β-D-Ribofuranosylamine, N-(6-amino-5-nitro-4-pyrimidinyl)-5-deoxy-5-fluoro-, 2,3-dibenzoate (9CI)
MF C23 H20 F N5 O7

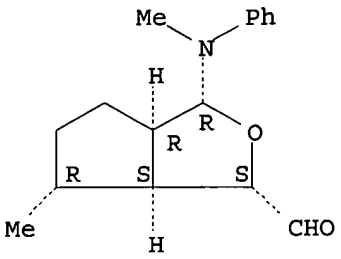
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 18 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 1H-Cyclopenta[c]furan-1-carboxaldehyde, hexahydro-6-methyl-3-(methylphenylamino)-, (1α,3α,3aα,6α,6aα)- (9CI)
MF C16 H21 N O2

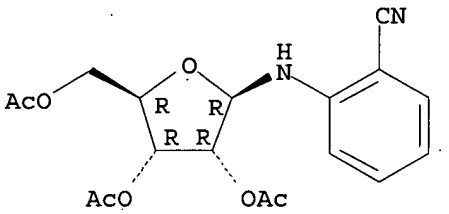
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 18 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzonitrile, 2-[(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)amino]- (9CI)
MF C18 H20 N2 O7

Absolute stereochemistry.

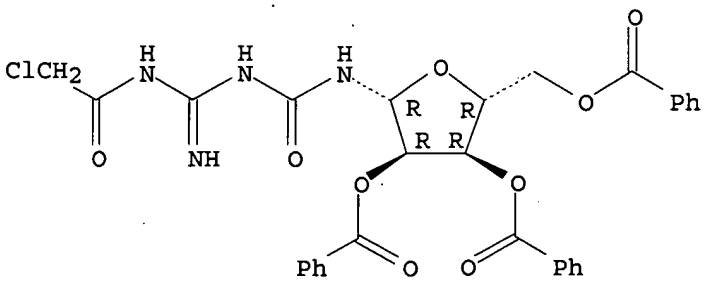


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):4

L2 18 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Acetamide, 2-chloro-N-[imino[[[(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)amino]carbonyl]amino]methyl]- (9CI)
MF C30 H27 Cl N4 O9

Absolute stereochemistry.

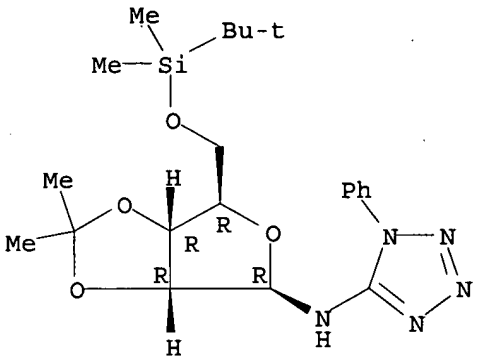


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 18 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN β-D-Ribofuranosylamine, 5-O-[(1,1-dimethylethyl)dimethylsilyl]-2,3-O-

(1-methylethylidene)-N-(1-phenyl-1H-tetrazol-5-yl)- (9CI)
MF C21 H33 N5 O4 Si

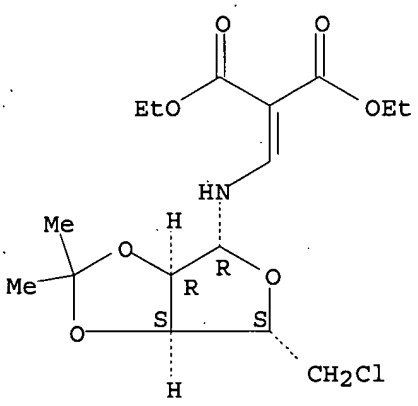
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 18 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Propanedioic acid, [[[5-chloro-5-deoxy-2,3-O-(1-methylethylidene)-β-D-ribofuranosyl]amino]methylene]-, diethyl ester (9CI)
MF C16 H24 Cl N O7

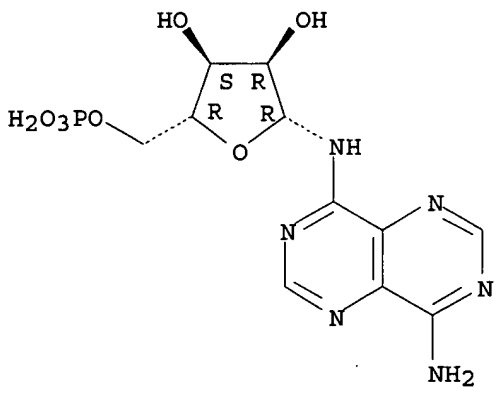
Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 18 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN β-D-Ribofuranosylamine, N-(8-aminopyrimido[5,4-d]pyrimidin-4-yl)-, 5-(dihydrogen phosphate), monosodium salt (9CI)
MF C11 H15 N6 O7 P . Na

Absolute stereochemistry.



● Na

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l1 sss full
FULL SEARCH INITIATED 16:44:24 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 274489 TO ITERATE

100.0% PROCESSED 274489 ITERATIONS 2501 ANSWERS
SEARCH TIME: 00.00.02

L3 2501 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	167.38	167.59

FILE 'CAPLUS' ENTERED AT 16:44:30 ON 23 OCT 2006
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 23 Oct 2006 VOL 145 ISS 18
FILE LAST UPDATED: 22 Oct 2006 (20061022/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4 1317 L3

```
=> s l4 and (nonsense(w)suppres?)
          7918 NONSENSE
        400106 SUPPRES?
           448 NONSENSE(W)SUPPRES?
L5           1 L4 AND (NONSENSE(W)SUPPRES?)

=> d l5 1 ti

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Use of nucleoside compounds for nonsense suppression
     and the treatment of genetic diseases


=> d l5 1 ti abs bib

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Use of nucleoside compounds for nonsense suppression
     and the treatment of genetic diseases
AB   The invention encompasses nucleoside compds., compns. comprising the
     compds. and methods for treating or preventing diseases associated with
     nonsense mutations of mRNA by administering these compds. or compns.
     Diseases that can be treated or prevented by compds. of the invention
     include, but are not limited to, cancer, autoimmune diseases, blood
     diseases, collagen diseases, diabetes, neurodegenerative diseases,
     cardiovascular diseases, pulmonary diseases, inflammatory diseases,
     lysosomal storage disease, tuberous sclerosis or central nervous system
     diseases.  The present invention is based in part on the discovery of
     small mols. that modulate premature translation termination and/or
     nonsense-mediated mRNA decay.
AN   2004:80704  CAPLUS
DN   140:122839
TI   Use of nucleoside compounds for nonsense suppression
     and the treatment of genetic diseases
IN   Wilde, Richard G.; Almstead, Neil G.; Welch, Ellen M.; Beckmann, Holger
PA   PTC Therapeutics, Inc., USA; Tularik Inc.
SO   PCT Int. Appl., 93 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 2004009610        A2    20040129    WO 2003-US23185        20030723
     WO 2004009610        A3    20051006
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
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             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
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     CA 2493816           AA    20040129    CA 2003-2493816        20030723
     AU 2003261237        A1    20040209    AU 2003-261237         20030723
     EP 1572709           A2    20050914    EP 2003-766015         20030723
     EP 1572709           A3    20051123
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI US 2002-398334P      P     20020724
     WO 2003-US23185      W     20030723
OS   MARPAT 140:122839
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=> file uspatfull
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY     SESSION
FULL ESTIMATED COST                                         7.43      175.02

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY     SESSION
CA SUBSCRIBER PRICE                                        -0.75       -0.75

FILE 'USPATFULL' ENTERED AT 16:45:11 ON 23 OCT 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 19 Oct 2006 (20061019/PD)
FILE LAST UPDATED: 19 Oct 2006 (20061019/ED)
HIGHEST GRANTED PATENT NUMBER: US7124445
HIGHEST APPLICATION PUBLICATION NUMBER: US2006236437
CA INDEXING IS CURRENT THROUGH 19 Oct 2006 (20061019/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 19 Oct 2006 (20061019/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006


=> s l3
L6          58 L3

=> s l6 and (nonsnese(w)suppres?)
            1 NONSNESE
       365999 SUPPRES?
            0 NONSNESE(W)SUPPRES?
L7          0 L6 AND (NONSNESE(W)SUPPRES?)

=> s l6 and (nonsenese(w)suppres?)
            0 NONSENESE
       365999 SUPPRES?
            0 NONSENESE(W)SUPPRES?
L8          0 L6 AND (NONSENESE(W)SUPPRES?)

=> s l6 and (nonsense(w)suppres?)
         4379 NONSENSE
       365999 SUPPRES?
          112 NONSENSE(W)SUPPRES?
L9          2 L6 AND (NONSENSE(W)SUPPRES?)

=> d l9 1-2 ti

L9   ANSWER 1 OF 2  USPATFULL on STN
TI     Use of nucleoside compounds for nonsense suppression
       and the treatment of genetic diseases

L9   ANSWER 2 OF 2  USPATFULL on STN
TI     Nucleoside compounds and their use for treating cancer and diseases
       associated with somatic mutations


=> file caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY     SESSION
FULL ESTIMATED COST                                        51.45      226.47

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                         0.00       -0.75

FILE 'CAPLUS' ENTERED AT 16:45:56 ON 23 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 23 Oct 2006 VOL 145 ISS 18
FILE LAST UPDATED: 22 Oct 2006 (20061022/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

```
=> s l4 and ((muscular(w)dystrophy) or readthrough or (cystic(w)fibrosis) or
glaucoma or (genetic(w)(disease or disorder)))
         25752 MUSCULAR
         12657 DYSTROPHY
          8644 MUSCULAR(W)DYSTROPHY
           986 READTHROUGH
         15664 CYSTIC
         34783 FIBROSIS
         11864 CYSTIC(W)FIBROSIS
          7189 GLAUCOMA
        745701 GENETIC
        896125 DISEASE
        252024 DISORDER
          4118 GENETIC(W)(DISEASE OR DISORDER)
L10          4 L4 AND ((MUSCULAR(W)DYSTROPHY) OR READTHROUGH OR (CYSTIC(W)FIBRO
               SIS) OR GLAUCOMA OR (GENETIC(W)(DISEASE OR DISORDER)))

=> d l10 1-4 ti

L10  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Preparation of nucleoside analogs for treating or preventing diseases
     associated with nonsense mutations of mRNA

L10  ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Use of nucleoside compounds for nonsense suppression and the treatment of
     genetic diseases

L10  ANSWER 3 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Fluorescent halide indicators

L10  ANSWER 4 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Long-wavelength iodide-sensitive fluorescent indicators for measurement of
     functional CFTR expression in cells


=> d l10 1 3 4 ti abs bib

L10  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Preparation of nucleoside analogs for treating or preventing diseases
     associated with nonsense mutations of mRNA
GI
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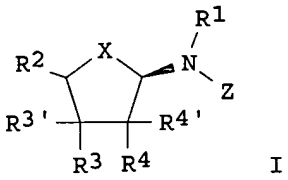
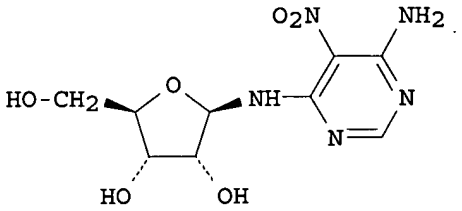


I



II

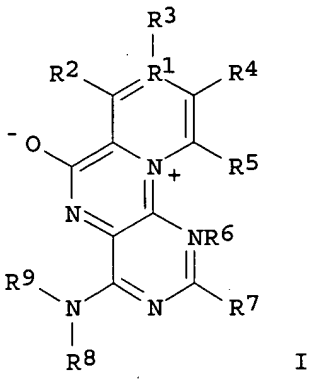
AB Nucleoside analogs I, wherein Z is (un)substituted alkyl, (un)substituted (un)substituted aryl, (un)substituted heteroaryl, (un)substituted cycloalkyl, (un)substituted heterocycle; X is CH, O, S, NH; R1 is H, (un)substituted alkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted cycloalkyl, (un)substituted heterocycle; R2 is (un)substituted alkyl, carboxy, amido, acyl, alkylcarbonyl, halogen, azide, alkyl amino, phosphate, phosphoester, alkyl ether; R3, R3', R4, R4' are independently (un)substituted ether, H, halogen, (un)substituted alkyl, (un)substituted (un)substituted aryl, (un)substituted heteroaryl, (un)substituted cycloalkyl, (un)substituted heterocycle are prepared for use in the treatment or prevention of diseases associated with nonsense mutations of mRNA. Thus, II was prepared and tested in a cell-based luciferase reporter assay containing a UGA premature termination codon that was stably transfected in 293T Human Embryonic Kidney cells (no data but very high potency and very high efficacy of protein synthesis). Further, I can be used as a prodrug in the treatment of autoimmune disease, blood diseases, collagen diseases, diabetes, neurodegenerative diseases, cardiovascular diseases, pulmonary diseases, inflammatory diseases, central nervous system diseases.

AN 2006:740594 CAPLUS
DN 145:167496
TI Preparation of nucleoside analogs for treating or preventing diseases associated with nonsense mutations of mRNA
IN Wilde, Richard G.; Almstead, Neil G.; Welch, Ellen M.; Beckmann, Holger
PA USA
SO U.S. Pat. Appl. Publ., 47 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006166926	A1	20060727	US 2005-48659	20050121
PRAI US 2005-48659		20050121		

OS MARPAT 145:167496

L10 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
TI Fluorescent halide indicators
GI



I

AB The invention provides methods and compns. for measuring ion concentration inside a cell by measuring fluorescence of I (R1 = C, N'; R2-9 = (un)substituted alkyl, alkenyl, aryl, heteroalkyl, heteroaryl, acyl, etc.). In particular embodiments, the measured ion is halide, particularly iodide, the cell contains a functional anion transport protein or channel, the method measures a change in fluorescence as a function of a predetd. condition such as the presence of a predetd. amount of a candidate modulator of ion transport in the cell (e.g. for drug screening) or the expression by the cell of a transgene such as the cystic fibrosis CFTR gene (e.g. to assess the efficacy of gene therapy).

AN 2000:707146 CAPLUS
DN 133:278350
TI Fluorescent halide indicators
IN Verkman, Alan S.; Biwersi, Joachim; Jayaraman, Sujatha
PA The Regents of the University of California, USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000058289	A1	20001005	WO 2000-US7799	20000324
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6201116	B1	20010313	US 1999-277354	19990326
PRAI	US 1999-277354	A	19990326		

OS MARPAT 133:278350
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
TI Long-wavelength iodide-sensitive fluorescent indicators for measurement of functional CFTR expression in cells
AB Limitations of available indicators [such as 6-methoxy-N-(3-sulfopropyl)quinolinium (SPQ)] for measurement of intracellular Cl- are their relatively dim fluorescence and need for UV excitation. A series of long-wavelength polar fluorophores was screened to identify compds. with Cl- and/or I- sensitivity, bright fluorescence, low toxicity, uniform loading of cytoplasm with minimal leakage, and chemical stability in cells.

The best compound found was 7-(β-D-ribofuranosylamino)-pyrido[2,1-h]-pteridin-11-ium-5-olate (LZQ). LZQ is brightly fluorescent with excitation and emission maxima at 400-470 and 490-560 nm, molar extinction 11,100 M-1·cm-1 (424 nm), and quantum yield 0.53. LZQ fluorescence is quenched by I- by a collisional mechanism (Stern-Volmer constant 60 M-1) and is not affected by other halides, nitrate, cations, or pH changes (pH 5-8). After LZQ loading into cytoplasm by hypotonic shock or overnight incubation, LZQ remained trapped in cells (leakage <3%/h). LZQ stained cytoplasm uniformly, remained chemical inert, did not bind to cytoplasmic components, and was photobleached by <1% during 1 h of continuous illumination. Cytoplasmic LZQ fluorescence was quenched selectively by I- (50% quenching at 38 mM I-). LZQ was used to measure forskolin-stimulated I-/Cl- and I-/NO3- exchange in cystic fibrosis transmembrane conductance regulator (CFTR)-expressing cell lines by fluorescence microscopy and microplate reader instrumentation using 96-well plates. The substantially improved optical and cellular properties of LZQ over existing indicators should permit the quant. anal. of CFTR function in gene delivery trials and high-throughput screening of compds. for correction of the cystic fibrosis phenotype.

AN 1999:767665 CAPLUS
DN 132:90258
TI Long-wavelength iodide-sensitive fluorescent indicators for measurement of functional CFTR expression in cells
AU Jayaraman, Sujatha; Teitler, Leah; Skalski, Bohdan; Verkman, A. S.
CS Departments of Medicine and Physiology, Cardiovascular Research Institute, University of California, San Francisco, CA, 94143-0521, USA
SO American Journal of Physiology (1999), 277(5, Pt. 1), C1008-C1018
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 16:42:54 ON 23 OCT 2006)

FILE 'REGISTRY' ENTERED AT 16:43:05 ON 23 OCT 2006
L1 STRUCTURE UPLOADED
L2 18 S L1 SSS SAM
L3 2501 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 16:44:30 ON 23 OCT 2006
L4 1317 S L3
L5 1 S L4 AND (NONSENSE(W)SUPPRES?)

FILE 'USPATFULL' ENTERED AT 16:45:11 ON 23 OCT 2006
L6 58 S L3
L7 0 S L6 AND (NONSNESE(W)SUPPRES?)
L8 0 S L6 AND (NONSENESE(W)SUPPRES?)
L9 2 S L6 AND (NONSENSE(W)SUPPRES?)

FILE 'CAPLUS' ENTERED AT 16:45:56 ON 23 OCT 2006
L10 4 S L4 AND ((MUSCULAR(W)DYSTROPHY) OR READTHROUGH OR (CYSTIC(W)FI

=> s l4 and (premature(w)stop)
30766 PREMATURE
39587 STOP
1762 PREMATURE(W)STOP
L11 0 L4 AND (PREMATURE(W)STOP)

=> s l4 and (stop(w)codon)

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         39587 STOP
         37627 CODON
          5402 STOP(W)CODON
L12           0 L4 AND (STOP(W)CODON)

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        38.11     264.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                        -2.25      -3.00

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
       AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
       CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
       DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 16:50:08 ON 23 OCT 2006

68 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s (adenosine(w)kinase) and ((nonsense(w)suppres?) or readthrough)
  24 FILES SEARCHED...
           7   FILE GENBANK
           1   FILE PROUSDDR
  56 FILES SEARCHED...

   2 FILES HAVE ONE OR MORE ANSWERS,    68 FILES SEARCHED IN STNINDEX

L13  QUE (ADENOSINE(W) KINASE) AND ((NONSENSE(W) SUPPRES?) OR READTHROUGH)

=> file prousddr
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         1.22     265.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                         0.00      -3.00

FILE 'PROUSDDR' ENTERED AT 16:51:19 ON 23 OCT 2006
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 FILE COVERS 1980 TO 2 Oct 2006 (20061002/ED)

=> s (adenosine(w)kinase) and ((nonsense(w)suppres?) or readthrough)
          1839 ADENOSINE
          8611 KINASE
            76 ADENOSINE(W)KINASE
            10 NONSENSE
          2806 SUPPRES?
             6 NONSENSE(W)SUPPRES?
             0 READTHROUGH
L14          1 (ADENOSINE(W)KINASE) AND ((NONSENSE(W)SUPPRES?) OR READTHROUGH)

=> d l14 1 ti abs bib
'ABS' IS NOT A VALID FORMAT FOR FILE 'PROUSDDR'

The following are valid formats:
```

The default display format is QRD.

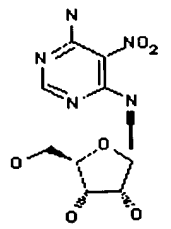
```
ALL ---- AN, DN, CN, RN, MF, PHP, STA, HDP(DSTA), CO, CC, ACTN,
         OS, ED(UP), STR, PROUS REFERENCE: RE, RTX,
         PATENT REFERENCES: TI, IN, PA, PI, PRAI, REFERENCE: RE
DALL --- Same as ALL with delimiters
IALL --- Indented ALL
BIB ---- AN, PROUS REFERENCE: RE, RTX,
         PATENT REFERENCES: TI, IN, PA, PI, PRAI,
         REFERENCE: RE
IBIB --- Indented BIB
IDE ---- AN, DN, CN, RN, MF, PHP, STA, HDP, CO, CC, OS, ED(UP), STR
IIDE --- Indented IDE
QRD ---- Query Related Data (AN, DN, CN, RN, MF, PHP, STA, HDP,
         CO, CC, ACTN, OS, ED, STR, plus all fields containing hit terms)
SAM ---- Same as TRI
SCAN --- CC, CO, RN, CN, ACTN
TRIAL -- (TRI) AN, CN, CO, CC, ACTN, OS
FREE --- Same as TRI
HIT ---- All fields containing hit terms
KWIC --- All hit terms plus 20 words on either side
OCC ---- List of display fields containing hit terms
```

Hit terms will be highlighted in all displayable fields.

To display a particular field or fields, enter the display field codes. For a list of display fields codes, enter 'HELP DFIELDS' at an arrow prompt (=>). Examples of formats include: 'IALL';
ENTER DISPLAY FORMAT (QRD):qrd

```
L14  ANSWER 1 OF 1  PROUSDDR COPYRIGHT 2006 PROUS SCIENCE on STN
AN   1988:4248     PROUSDDR
DN   142010
CN   6-Amino-5-nitro-4-(beta-D-ribofuranosylamino)pyrimidine
CN   GENERIC NAME: Clitocine
RN   105798-74-1
MF   C9 H13 N5 O6
PHP  M.p. 230-1 C
HDP  BIOLOGICAL TESTING
CO   ORIGINATOR: Valeant
CC   Oncolytic Drugs
ACTN Antimetabolites
ED   Entered STN: 9 May 2004
     Last Updated on STN: 2 May 2006
```

STRUCTURE:




```
RTX  RefID: 61515
     ACTION - Antineoplastic agent, isolated from the mushroom Clitocybe
     inversa, which inhibits the growth of L1210 murine lymphocytic leukemia,
     WI-L2 human B-cell lymphoblastic leukemia and CCRF-CEM human TT-cell
     lymphoblastic leukemia in vitro (ID50 = 0.03 mcM), and also is a substrate
     and inhibitor of adenosine kinase (Ki = 3 mcM).
```

PATENT REFERENCES:

TI Use of nucleoside compounds for nonsense suppression
and the treatment of genetic diseases
IN Wilde, R.G.; Almstead, N.G.; Welch, E.M.; Beckmann, H.
PA Amgen
PA PTC Therapeutics
PI EP 1572709 20050914
WO 2004009610 20040129
PRAI US 2002-398334 20020724

START LOCAL KERMIT RECEIVE PROCESS

BINARY DATA HAS BEEN DOWNLOADED TO MULTIPLE FILES 'IMAGEnnn.TIF'

=> log hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	23.41	289.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-3.00

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 16:51:52 ON 23 OCT 2006

```
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Welcome to STN International!  Enter x:x

LOGINID:SSPTAEXO1623

PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'PROUSDDR' AT 17:09:50 ON 23 OCT 2006
FILE 'PROUSDDR' ENTERED AT 17:09:50 ON 23 OCT 2006
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    23.41     289.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -3.00

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    23.41     289.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -3.00

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
       AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
       CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
       DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 17:10:06 ON 23 OCT 2006

68 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s (gene(w)therapy) and (autoimmun? or arthrtis or (multiple(w)sclerosis) or
(Alzheim?) or parkinson? or hemophilia or (ataxia-telangiectasia) or thalassemia or
(kidney(w)stones))
          6   FILE ADISCTI
         52   FILE ADISINSIGHT
         26   FILE ADISNEWS
          7   FILE AGRICOLA
          5   FILE ANTE
        331   FILE BIOENG
       1502   FILE BIOSIS
       7290   FILE BIOTECHABS
       7290   FILE BIOTECHDS
       1426   FILE BIOTECHNO
  13 FILES SEARCHED...
         19   FILE CABA
       3295   FILE CAPLUS
         64   FILE CEABA-VTB
        195   FILE CIN
         27   FILE CONFSCI
          1   FILE CROPU
        362   FILE DDFU
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   397280   FILE DGENE
 23 FILES SEARCHED...
       61   FILE DISSABS
      400   FILE DRUGU
       25   FILE EMBAL
     2232   FILE EMBASE
      938   FILE ESBIOBASE
        1   FILE FROSTI
       53   FILE GENBANK
      421   FILE IFIPAT
      186   FILE IMSDRUGNEWS
 39 FILES SEARCHED...
      116   FILE IMSRESEARCH
      372   FILE JICST-EPLUS
      460   FILE LIFESCI
     1760   FILE MEDLINE
       15   FILE NTIS
      883   FILE PASCAL
       62   FILE PCTGEN
       43   FILE PHAR
       93   FILE PHARMAML
        1   FILE PHIC
      360   FILE PHIN
     2436   FILE PROMT
        4   FILE PROUSDDR
 56 FILES SEARCHED...
        1   FILE RDISCLOSURE
     1951   FILE SCISEARCH
      864   FILE TOXCENTER
    14324   FILE USPATFULL
     1527   FILE USPAT2
     5447   FILE WPIDS
       32   FILE WPIFV
     5447   FILE WPINDEX

 48 FILES HAVE ONE OR MORE ANSWERS,   68 FILES SEARCHED IN STNINDEX

L15  QUE (GENE(W) THERAPY) AND (AUTOIMMUN? OR ARTHRTIS OR (MULTIPLE(W) SCLEROSI
       S) OR (ALZHEIM?) OR PARKINSON? OR HEMOPHILIA OR (ATAXIA-TELANGIECTASIA
       ) OR THALASSEMIA OR (KIDNEY(W) STONES))

=> file embase medline caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    3.66     292.87

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                    0.00      -3.00

FILE 'EMBASE' ENTERED AT 17:13:44 ON 23 OCT 2006
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FILE 'MEDLINE' ENTERED AT 17:13:44 ON 23 OCT 2006

FILE 'CAPLUS' ENTERED AT 17:13:44 ON 23 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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=> s (gene(w)therapy) and (autoimmun? or arthrtis or (multiple(w)sclerosis) or
(Alzheim?) or parkinson? or hemophilia or (ataxia-telangiectasia) or thalassemia or
(kidney(w)stones))
L16        7287 (GENE(W) THERAPY) AND (AUTOIMMUN? OR ARTHRTIS OR (MULTIPLE(W)
               SCLEROSIS) OR (ALZHEIM?) OR PARKINSON? OR HEMOPHILIA OR (ATAXIA-
```

TELANGIECTASIA) OR THALASSEMIA OR (KIDNEY(W) STONES))

=> s l16 and clitocine
L17 0 L16 AND CLITOCINE

=> s l16 and (nonsense)
L18 14 L16 AND (NONSENSE)

=> d l18 1-14 ti

L18 ANSWER 1 OF 14 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
TI Treatment of experimental autoimmune encephalomyelitis with antisense oligonucleotides against the low affinity neurotrophin receptor.

L18 ANSWER 2 OF 14 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
TI Construction of a functional human suppressor tRNA gene: An approach to gene therapy for β-thalassaemia.

L18 ANSWER 3 OF 14 MEDLINE on STN
TI Novel hemophilia B mouse models exhibiting a range of mutations in the Factor IX gene.

L18 ANSWER 4 OF 14 MEDLINE on STN
TI Treatment of experimental autoimmune encephalomyelitis with antisense oligonucleotides against the low affinity neurotrophin receptor.

L18 ANSWER 5 OF 14 MEDLINE on STN
TI [Molecular genetics of hemophilia A].
Genetica molecular de la hemofilia A.

L18 ANSWER 6 OF 14 MEDLINE on STN
TI Construction of a functional human suppressor tRNA gene: an approach to gene therapy for beta-thalassaemia.

L18 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI RNA splicing manipulation: Strategies to modify gene expression for a variety of therapeutic outcomes

L18 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Components of nonsense-mediated mRNA decay (NMD) complex, and methods of drug screening and treating disorders related to NMD by modulating NMD

L18 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Treatment of experimental autoimmune encephalomyelitis with antisense oligonucleotides against the low affinity neurotrophin receptor

L18 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI A protein regulating decay of mRNAs containing nonsense codons and controlling the decay of foreign mRNAs in expression hosts using derivatives of the protein

L18 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Positional cloning and sequence of the APECED gene associated with autoimmune polyendocrinopathy syndrome type I

L18 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Molecular genetics of hemophilia A

L18 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Gene therapy using homologous recombination for mutation correction

L18 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Construction of a functional human suppressor tRNA gene: an approach to gene therapy for β- thalassemia

=> d l18 1-18 ti abs bib

L18 ANSWER 1 OF 14 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
TI Treatment of experimental autoimmune encephalomyelitis with antisense oligonucleotides against the low affinity neurotrophin receptor.
AB Upregulated expression of the low-affinity neurotrophin receptor (p75) in the central nervous system (CNS) during experimental autoimmune encephalomyelitis (EAE) has recently been demonstrated. To investigate whether p75 plays a role in disease pathogenesis, we adopted a gene therapy approach, utilizing antisense oligonucleotides to downregulate p75 expression during EAE. Phosphorothioate antisense oligonucleotides (AS), nonsense oligonucleotides (NS) or phosphate buffered saline (PBS) were injected daily for 18 days after immunization of SJL/J (H-2s)-mice with myelin proteolipid protein (PLP) peptide 139-151. In the AS group, there was a statistically significant reduction in both the mean maximal disease score (1.85 in the AS, 2.94 in the NS and 2.75 in the PBS-groups, respectively, $P < 0.025$) and in the cumulative disease incidence (.simeq. 60% in the AS group and .simeq. 90% in the control groups). Histological and immunohistochemical analysis showed reduced inflammation and demyelination, as well as reduced p75 expression at the blood-brain barrier (BBB) in the AS-treated mice in comparison with both control groups. There was no difference, however, in p75 expression on neural cells within the CNS between the three groups of mice. We conclude that p75 could play a proactive role in the pathogenesis of EAE and may exert its effect at the level of the BBB. (C) 2000 Wiley-Liss, Inc.
AN 2000358373 EMBASE
TI Treatment of experimental autoimmune encephalomyelitis with antisense oligonucleotides against the low affinity neurotrophin receptor.
AU Soilu-Hanninen M.; Epa R.; Shipham K.; Butzkueven H.; Bucci T.; Barrett G.; Bartlett P.F.; Kilpatrick T.J.
CS Dr. T.J. Kilpatrick, Development and Neurobiology Group, Walter/Eliza Hall Inst. of Med. Res., Royal Melbourne Hospital, Parkville, Vic. 3050, Australia. kilpatrick@wehi.edu.au
SO Journal of Neuroscience Research, (15 Mar 2000) Vol. 59, No. 6, pp. 712-721. .
Refs: 41
ISSN: 0360-4012 CODEN: JNREDK
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 2 Nov 2000
Last Updated on STN: 2 Nov 2000

L18 ANSWER 2 OF 14 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
TI Construction of a functional human suppressor tRNA gene: An approach to gene therapy for β-thalassaemia.
AB A human rRNA(Lys) gene was converted to an amber suppressor by site-specific mutagenesis of the anticodon. The mutated tRNA(Lys) gene directed synthesis of a tRNA suppressed the UAG amber nonsense mutation in β0 thalassaemia mRNA. Such genes may be used to detect other nonsense mutations in mammalian cells and may provide an approach to gene therapy for β0 thalassaemia due to nonsense mutations.

AN 82206283 EMBASE
DN 1982206283
TI Construction of a functional human suppressor tRNA gene: An approach to gene therapy for β-thalassaemia.
AU Temple G.F.; Dozy A.M.; Roy K.L.; Kan Y.W.
CS Howard Hughes Med. Inst. Lab., Univ. California, San Francisco, CA 94143, United States
SO Nature, (1982) Vol. 296, No. 5857, pp. 537-540. .
CODEN: NATUAS
CY United Kingdom
DT Journal
FS 022 Human Genetics
025 Hematology
LA English
ED Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991

L18 ANSWER 3 OF 14 MEDLINE on STN
TI Novel hemophilia B mouse models exhibiting a range of mutations in the Factor IX gene.
AB Animal models have been critical to the development of novel therapeutics in hemophilia. A deficiency of current murine models of hemophilia B is that they are all due to gene deletions, a type of mutation that is relatively rare in the human hemophilia population. We generated mice with a range of mutations in the Factor IX (F.IX) gene; these more faithfully reflect the types of mutations that cause disease in the human population. Transgenic mice expressing either wild-type human F.IX (hF.IX), or F.IX variants with premature translation termination codons, or missense mutations, under the control of the murine transthyretin promoter, were generated and crossed with mice carrying a large deletion of the murine F.IX gene. Gene copy number, F.IX transcript levels in the liver, intrahepatocyte protein expression, and circulating levels of F.IX protein in the mice were determined and compared with data generated by transient transfection assays using the same F.IX variants. Mice were injected with a viral vector expressing hF.IX and displayed a range of immune responses to the transgene product, depending on the underlying mutation. These new mouse models faithfully mimic the mutations causing human disease, and will prove useful for testing novel therapies for hemophilia.
AN 2004527510 MEDLINE
DN PubMed ID: 15217833
TI Novel hemophilia B mouse models exhibiting a range of mutations in the Factor IX gene.
AU Sabatino Denise E; Armstrong Elina; Edmonson Shyrie; Liu Yi-Lin; Pleimes Marc; Schuettrumpf Joerg; Fitzgerald Julie; Herzog Roland W; Arruda Valder R; High Katherine A
CS Department of Pediatrics, Graduate Program in Gene Therapy, University of Pennsylvania School of Medicine, Philadelphia, USA.
NC K01 DK60580 (NIDDK)
P01 HL64190 (NHLBI)
R01A1/HL51390 (NHLBI)
U01 HL66948 (NHLBI)
SO Blood, (2004 Nov 1) Vol. 104, No. 9, pp. 2767-74. Electronic Publication: 2004-06-24.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200412
ED Entered STN: 23 Oct 2004
Last Updated on STN: 20 Dec 2004
Entered Medline: 14 Dec 2004

L18 ANSWER 4 OF 14 MEDLINE on STN

TI Treatment of experimental autoimmune encephalomyelitis with antisense oligonucleotides against the low affinity neurotrophin receptor.

AB Upregulated expression of the low-affinity neurotrophin receptor (p75) in the central nervous system (CNS) during experimental autoimmune encephalomyelitis (EAE) has recently been demonstrated. To investigate whether p75 plays a role in disease pathogenesis, we adopted a gene therapy approach, utilizing antisense oligonucleotides to downregulate p75 expression during EAE. Phosphorothioate antisense oligonucleotides (AS), nonsense oligonucleotides (NS) or phosphate buffered saline (PBS) were injected daily for 18 days after immunization of SJL/J (H-2s)-mice with myelin proteolipid protein (PLP) peptide 139-151. In the AS group, there was a statistically significant reduction in both the mean maximal disease score (1.85 in the AS, 2.94 in the NS and 2.75 in the PBS-groups, respectively, $P < 0.025$) and in the cumulative disease incidence (approximately 60% in the AS group and approximately 90% in the control groups). Histological and immunohistochemical analysis showed reduced inflammation and demyelination, as well as reduced p75 expression at the blood-brain barrier (BBB) in the AS-treated mice in comparison with both control groups. There was no difference, however, in p75 expression on neural cells within the CNS between the three groups of mice. We conclude that p75 could play a proactive role in the pathogenesis of EAE and may exert its effect at the level of the BBB.

AN 2000164869 MEDLINE
DN PubMed ID: 10700008

TI Treatment of experimental autoimmune encephalomyelitis with antisense oligonucleotides against the low affinity neurotrophin receptor.

AU Soilu-Hanninen M; Epa R; Shipham K; Butzkueven H; Bucci T; Barrett G; Bartlett P F; Kilpatrick T J
CS The Walter and Eliza Hall Institute of Medical Research, The Royal Melbourne Hospital, Parkville, Victoria, Australia.

SO Journal of neuroscience research, (2000 Mar 15) Vol. 59, No. 6, pp. 712-21.
Journal code: 7600111. ISSN: 0360-4012.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
ED Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000
Entered Medline: 13 Apr 2000

L18 ANSWER 5 OF 14 MEDLINE on STN

TI [Molecular genetics of hemophilia A].
Genetica molecular de la hemofilia A.

AB Hemophilia A (HemA), an X linked genetic disease, is the most common coagulation disorder with an incidence of about 1-2 in 10,000 males and is caused by mutations in the factor VIII (FVIII) coagulation gene. Firstly, some clinical aspects of the HemA are presented: the current methods to assess both the amount and activity of FVIII, the severity range observed and the presence of inhibitor antibodies against the therapeutic FVIII. Follows a discussion of the relationship of the structural domains of the FVIII protein (Figure 1), the aminoacid sequence and their functions. An activation-inactivation model of the successive peptide bonds cleavages of the FVIII is also presented (Figure 2). After the cloning of the FVIII gene in 1984, almost all types of HemA causing mutations have been characterized. However, the size and complexity of this gene prevented a screening of the full range of mutations for an accurate molecular diagnosis. Moreover, most of the patients with moderate and mild disease have missense mutations whereas approximately half of severe patients have nonsense, frameshift, and some missense mutations. There are also less frequently mutations such as deletions and insertions leading to severe phenotype and mutations

affecting mRNA splicing and duplications causing both severe and mild HemA. In order to give genetic counselling in HemA families, studies at the DNA level using intragenic and/ or extragenic polymorphism analysis have been used. But this approach is not entirely satisfactory because it fails in several situations. Most of the causing mutations described above are private, and they have been found in only a few unrelated families. Recently, a common molecular inversion of the FVIII gene was identified in 50% of unrelated patients with severe HemA. The copies of a particular DNA sequence (termed F8A gene). One copy is located within intron 22 of the FVIII gene and the other two, 500 kb upstream. An homologous recombination mechanism was proposed for the inversion between an intragenic copy of the F8A gene and either the distal (80% of the inversion) or the proximal copy (20%). Both of these inversions lead to severe HemA because no intact FVIII is produced and can be easily diagnosed by Southern blot analysis. This inversion originates almost exclusively in male germ cells, because pairing Xq with its homologous in female meiosis would probably inhibit the proposed intrachromosome recombination. The molecular analysis of the inversion of intron 22 is now considered as the first line for families with severe HemA patients. In recent years the treatment of patients with hemophilia A and B has been intravenous injection of FVIII or FIX concentrates, respectively. This regimen of regular injection of plasmatic proteins bears a high risk of infection by contaminating viruses (HIV, HBV, etc). Future treatment for patients with hemophilia may include the use of either gene therapy or recombinant coagulation factors. Both strategies would completely avoid the infection risk offering a safe and effective treatment for the disease. Recombinant factors, obtained by genetic engineering methods, provide a renewable and unlimited source of FVIII or FIX. The clinical trials of recombinant factors have already started in mid-1995 giving positive results. On the other hand, gene therapy for hemophilia is now in the pre-clinical stage but offers the prospect of a cure for the disease, thus potentially freeing patients from regular injections of the lacking protein. However, experiments in animal models suggest that it may be difficult to obtain adequate therapeutic levels of factors for long periods of time. Recently, a retroviral-mediated gene delivery of human FVIII in mice has been reported using the ex vivo strategy of gene therapy. Therapeutic levels of FVIII in the circulation were obtained for > 1 week and it was also observed that the capacity of primary cells to deliver FVIII in blood was strongly dependent on

AN 97384041 MEDLINE
DN PubMed ID: 9239887
TI [Molecular genetics of hemophilia A].
Genetica molecular de la hemofilia A.
AU De Brasi C D; Slavutsky I R; Larripa I B
CS Departamento de Genetica, Academia Nacional de Medicina, Buenos Aires, Argentina.
SO Medicina, (1996) Vol. 56, No. 5 Pt 1, pp. 509-17. Ref: 32
Journal code: 0204271. ISSN: 0025-7680.
CY Argentina
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA Spanish
FS Priority Journals
EM 199710
ED Entered STN: 24 Dec 1997
Last Updated on STN: 29 Jan 1999
Entered Medline: 27 Oct 1997

L18 ANSWER 6 OF 14 MEDLINE on STN
TI Construction of a functional human suppressor tRNA gene: an approach to gene therapy for beta-thalassaemia.
AB A human tRNALys gene was converted to an amber suppressor by site-specific mutagenesis of the anticodon. The mutated tRNALys gene directed synthesis of a tRNA that suppressed the UAG amber nonsense mutation in

beta O thalassemia mRNA. Such genes may be used to detect other nonsense mutations in mammalian cells and may provide an approach to gene therapy for beta O thalassaemia due to nonsense mutations.

AN 82173152 MEDLINE
DN PubMed ID: 6803169
TI Construction of a functional human suppressor tRNA gene: an approach to gene therapy for beta-thalassaemia.
AU Temple G F; Dozy A M; Roy K L; Kan Y W
SO Nature, (1982 Apr 8) Vol. 296, No. 5857, pp. 537-40.
Journal code: 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198206
ED Entered STN: 17 Mar 1990
Last Updated on STN: 17 Mar 1990
Entered Medline: 21 Jun 1982

L18 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI RNA splicing manipulation: Strategies to modify gene expression for a variety of therapeutic outcomes
AB A review. Antisense oligonucleotides initially offered great hope as specific compds. to modify gene expression, primarily through RNaseH induced degradation of the target transcript. Expansion of the field led to new chemistries capable of invoking different mechanisms, including suppression of protein synthesis by translational blockade, and there is now a major interest in downregulation of gene expression using short interfering RNAs to induce RNA silencing. Naturally occurring microRNAs have been implicated in the regulation of gene expression. This review considers examples of antisense oligonucleotides redirecting the process of exon recognition and intron removal during gene transcript splicing. While suppression of gene expression is necessary to address some conditions, it appears likely that there may be many more clin. applications for antisense oligonucleotides in re-directing splicing patterns. Pre-mRNA splicing is a tightly coordinated, multifactorial process, which can be disrupted by antisense oligonucleotides in a highly specific manner, allowing either suppression of aberrant splicing, bypass of nonsense or frame-shifting mutations or alteration of spliceoform ratios. Manipulation of splicing patterns has been applied to a diverse range of conditions, including β- thalassemia, Duchenne muscular dystrophy, spinal muscular atrophy and certain cancers. Alternative exon usage has been identified as a major mechanism for generating diversity from a limited repertoire of genes in higher eukaryotes. Considering that up to 75% of all human primary gene transcripts are reported to be alternatively spliced, intervention at the level of pre-mRNA processing is likely to become increasingly significant in the fight against genetic and acquired disorders.
AN 2005:1093515 CAPLUS
DN 144:247820
TI RNA splicing manipulation: Strategies to modify gene expression for a variety of therapeutic outcomes
AU Wilton, Steve D.; Fletcher, Susan
CS Experimental Molecular Medicine Group, Centre for Neuromuscular and Neurological Disorders, University of Western Australia, Australia
SO Current Gene Therapy (2005), 5(5), 467-483
CODEN: CGTUAH; ISSN: 1566-5232
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
RE.CNT 161 THERE ARE 161 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

TI Components of nonsense-mediated mRNA decay (NMD) complex, and methods of drug screening and treating disorders related to NMD by modulating NMD

AB Disclosed are compns. and methods relating to nonsense mediated decay (NMD) particularly in the 'pioneer' round of translation. Disclosed are methods of screening for a substance that modulates a NMD complex. The complex optionally comprises Upf2, Upf3, Upf3X, PABP2, CBP20, CBP80, hSmg5/7a, hSmg5/7b, hSmg5/7c, poly(A)RNase (PARN), Dcp2, PM/Scl100, Rat1, Xrn1, Rrp41 or a combination thereof. The present invention provides methods of treating disorders relating to NMD and methods of screening substances for use in the study of or treatment of conditions relating to NMD.

AN 2004:371048 CAPLUS

DN 140:368631

TI Components of nonsense-mediated mRNA decay (NMD) complex, and methods of drug screening and treating disorders related to NMD by modulating NMD

IN Maquat, Lynne E.

PA University of Rochester, USA

SO PCT Int. Appl., 192 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004037976	A2	20040506	WO 2003-US26166	20030821
	WO 2004037976	A3	20040805		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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	AU 2003298555	A1	20040513	AU 2003-298555	20030821
	US 2006154883	A1	20060713	US 2006-525273	20060207
PRAI	US 2002-405602P	P	20020822		
	WO 2003-US26166	W	20030821		

L18 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

TI Treatment of experimental autoimmune encephalomyelitis with antisense oligonucleotides against the low affinity neurotrophin receptor

AB Upregulated expression of the low-affinity neurotrophin receptor (p75) in the central nervous system (CNS) during exptl. autoimmune encephalomyelitis (EAE) has recently been demonstrated. To investigate whether p75 plays a role in disease pathogenesis, the authors adopted a gene therapy approach, utilizing antisense oligonucleotides to downregulate p75 expression during EAE. Phosphorothioate antisense oligonucleotides (AS), nonsense oligonucleotides (NS) or phosphate buffered saline (PBS) were injected daily for 18 days after immunization of SJL/J (H-2s)-mice with myelin proteolipid protein (PLP) peptide 139-151. In the AS group, there was a statistically significant reduction in both the mean maximal disease score (1.85 in the AS, 2.94 in the NS and 2.75 in the PBS-groups, resp.) and in the cumulative disease incidence (≈60% in the AS group and ≈90% in the control groups). Histol. and immunohistochem. anal. showed reduced inflammation and demyelination, as well as reduced p75 expression at the blood-brain barrier (BBB) in the AS-treated mice in comparison with both control groups. There was no difference, however, in p75 expression on neural cells within the CNS between the three groups of mice. The authors conclude that p75 could play a proactive role in the

pathogenesis of EAE and may exert its effect at the level of the BBB.
AN 2000:182651 CAPLUS
DN 132:342990
TI Treatment of experimental autoimmune encephalomyelitis with antisense oligonucleotides against the low affinity neurotrophin receptor
AU Soilu-Hanninen, Merja; Epa, Ruwan; Shipham, Kylie; Butzkueven, Helmut; Bucci, Tamara; Barrett, Graham; Bartlett, Perry F.; Kilpatrick, Trevor J.
CS The Walter and Eliza Hall Institute of Medical Research, The Royal Melbourne Hospital, Parkville, 3050, Australia
SO Journal of Neuroscience Research (2000), 59(6), 712-721
CODEN: JNREDK; ISSN: 0360-4012
PB Wiley-Liss, Inc.
DT Journal
LA English
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI A protein regulating decay of mRNAs containing nonsense codons and controlling the decay of foreign mRNAs in expression hosts using derivatives of the protein
AB A Saccharomyces cerevisiae gene, NMD2, named after its role in the nonsense-mediated mRNA decay pathway, and the gene product are characterized. The NMD2 gene product binds to another protein involved in this decay pathway, the UPF1 gene product. A C-terminal fragment of the NMD2 protein is shown to bind the UPF1 protein and when a gene for this fragment is overexpressed in the host cell, the fragment inhibits the function of UPF1 and blocks the nonsense-mediated mRNA decay pathway. This may be used to block the degradation of mRNAs containing a nonsense codon that would normally cause an increase in the transcript decay rate. Such stabilization of a transcript is useful in manufacture the manufacture of proteins encoded by genes containing an unexpected
nonsense codon, e.g. in the manufacture of a fragment of a protein generated by introduction of a nonsense mutation into a gene. The invention also relates to methods of identifying mols. that inhibit the nonsense-mediated mRNA decay pathway, and the use of such mols. for treatment of disorders associated with nonsense mutations.
AN 1999:286119 CAPLUS
DN 130:308197
TI A protein regulating decay of mRNAs containing nonsense codons and controlling the decay of foreign mRNAs in expression hosts using derivatives of the protein
IN He, Feng; Jacobson, Allan S.
PA University of Massachusetts, USA
SO PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9920797	A1	19990429	WO 1998-US22365	19981021
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9911140	A1	19990510	AU 1999-11140	19981021
PRAI	US 1997-955472	A	19971021		
	WO 1998-US22365	W	19981021		

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Positional cloning and sequence of the APECED gene associated with

autoimmune polyendocrinopathy syndrome type I

AB The present invention relates to a novel gene, a novel protein encoded by said gene, a mutated form of the gene and to diagnostic and therapeutic uses of the gene or a mutated form thereof. More specifically, the present invention relates to a novel gene defective in autoimmune polyendocrinopathy syndrome type I (APS I), also called autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) (MIM Number 240,300). Autoimmune polyglandular syndrome type I (APS 1, also called APECED) is an autosomal-recessive disorder that maps to human chromosome 21q22.3 between markers D21S49 and D21S171 by linkage studies. A novel gene was isolated from this region, AIRE (autoimmune regulator), which encodes a protein containing motifs suggestive of a transcription factor including two zinc-finger (PHD-finger) motifs, a proline-rich region and three LXXLL motifs. Two mutations, a C→T substitution that changes the Arg 257 (CGA) to a stop codon (TGA) and an A→G substitution that changes the Lys 83 (AAG) to a Glu codon (GAG), were found in this novel gene in Swiss and Finnish APECED patients. The Arg257stop (R257X) is the predominant mutation in Finnish APECED patients, accounting for 10/12 alleles studied. These results indicate that this gene is responsible for the pathogenesis of APECED. The identification of the gene defective in APECED should facilitate the genetic diagnosis and potential treatment of the disease and further enhance our general understanding of the mechanisms underlying autoimmune diseases.

AN 1999:222961 CAPLUS

DN 130:247887

TI Positional cloning and sequence of the APECED gene associated with autoimmune polyendocrinopathy syndrome type I

IN Krohn, Kai; Heino, Maarit; Peterson, Part; Scott, Hamish; Antonarakis, Stylianos; Lalioti, Maria; Shimizu, Nobuyoshi; Kudoh, Jun

PA Finnish Immunotechnology Ltd., Finland

SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9915559	A1	19990401	WO 1998-FI749	19980923
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9893502	A1	19990412	AU 1998-93502	19980923
	EP 1017718	A1	20000712	EP 1998-946476	19980923
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	FI 1997-3762	A	19970923		
	WO 1998-FI749	W	19980923		

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

TI Molecular genetics of hemophilia A

AB A review with 32 refs. Hemophilia A (HemA), an X-linked genetic disease, is the most common coagulation disorder with an incidence of about 1-2 in 10,000 males and is caused by mutations in the factor VIII (FVIII) coagulation gene. Firstly, some clin. aspects of the HemA are presented: the current methods to assess both the amount and activity of FVIII, the severity range observed, and the presence of inhibitor antibodies against the therapeutic FVIII. A discussion of the relation of the

structural domains of the FVIII protein and of the amino acid sequence and their functions follows. An activation-inactivation model of the successive peptide bonds cleavages of the FVIII is also presented. After the cloning of the FVIII gene in 1984, almost all types of HemA causing mutations have been characterized. However, the size and complexity of this gene prevented a screening of the full range of mutations for an accurate mol. diagnosis. Moreover, most of the patients with moderate and mild disease have missense mutations, whereas approx. half of severe patients have nonsense, frameshift, and some missense mutations. There are also less frequently mutations such as deletions and insertions leading to severe phenotype and mutations affecting mRNA splicing and duplications causing both severe and mild HemA. In genetic counseling of HemA families, studies at the DNA level using intragenic and/or extragenic polymorphism anal. have been used. But this approach is not entirely satisfactory because it fails in several situations. Most of the causing mutations described above are private, and they have been found in only a few unrelated families. Recently, a common mol. inversion of the FVIII gene was identified in 50% of unrelated patients with severe HemA. The inversion is mediated by the presence of three copies of a particular DNA sequence (termed F8A gene). One copy is located within intron 22 of the FVIII gene and the other two, 500 kb upstream. An homologous recombination mechanism was proposed for the inversion between an intragenic copy of the F8A gene and either the distal (80% of the inversion) or the proximal copy (20%). Both of these inversions lead to severe HemA because no intact FVIII is produced and can be easily diagnosed by Southern blot anal. This inversion originates almost exclusively in male germ cells, because pairing Xq with its homolog in female meiosis would probably inhibit the proposed intrachromosome recombination. The mol. anal. of the inversion of intron 22 is now considered as the first line for families with severe HemA patients. In recent years, the treatment of patients with hemophilia A and B has been i.v. injection of FVIII or FIX concs., resp. This regimen of regular injection of plasmatic proteins bears a high risk of infection by contaminating viruses (HIV, HBV, etc.). Future treatment for patients with hemophilia may include the use of either gene therapy or recombinant coagulation factors. Both strategies would completely avoid the infection risk offering a safe and effective treatment for the disease. Recombinant factors, obtained by genetic engineering methods, provide a renewable and unlimited source of FVIII or FIX. The clin. trials of recombinant factors have already started in mid-1995 giving pos. results. Gene therapy for hemophilia is now in the pre-clin. stage but offers the prospect of a cure for the disease, thus potentially freeing patients from regular injections of the lacking protein. However, expts. in animal models suggest that it may be difficult to obtain adequate therapeutic levels of factors for long periods of time. Recently, a retroviral-mediated gene delivery of human FVIII in mice has been reported using the ex vivo strategy of gene therapy. Therapeutic levels of FVIII in the circulation were obtained for >1 wk and it was also observed that the capacity of primary cells to deliver FVIII in blood was strongly dependent on the site of implantation. Although much work remains to be done, these pos. results are encouraging for the future of gene therapy for this relatively common genetic disease.

AN 1997:137032 CAPLUS
DN 126:184435
TI Molecular genetics of hemophilia A
AU De Brasi, Carlos D.; Slavutsky, Irma R.; Larripa, Irene B.
CS Dep. Genet., Acad. Nacional Med., Buenos Aires, Argent.
SO Medicina (Buenos Aires) (1996), 56(5/1), 509-517
CODEN: MEDCAD; ISSN: 0025-7680
PB Sociedad Argentina de Investigacion Clinica
DT Journal; General Review
LA Spanish

L18 ANSWER 13 OF 14 CAPLUS

TI Gene therapy using homologous recombination for mutation correction

AB A method to correct is provided to correct the mutation(s) behind a genetic disease in the genome of somatic cells derived from an individual afflicted with this disease by contacting the cells with the corresponding non-mutant DNA-fragment to allow it to undergo homologous recombination and, thus, replace a DNA sequence of the somatic cell genome, wherein the mutation(s) is(are) located. The cells obtained can be administered to an individual as a treatment of the disease. A DNA-liposome suspension comprising the non-mutant DNA-fragment can be used as a DNA-vehicle in the process. In addition, it can be administered to an individual to obtain correction of mutation(s) by in vivo integration of the said DNA into a mutated gene by homologous recombination. Diseases for which the responsible mutations have been identified and which, thus, could be treated by the above method are autosomal and X-linked genetic disorders, such as von Willebrand's disease, sickle-cell anemia, β-thalassemia, hemophilia A and B, and cystic fibrosis. Thus, lymphocytes from a patient with a homozygous nonsense mutation (R1659X/R1659X) in exon 28 of the von Willebrand factor gene were used to establish Epstein-Barr virus-transformed lymphocytes. A non-mutant DNA fragment comprised of the whole exon 28 and parts of introns 27 and 28 and corresponding to the mutant region, was amplified from normal individuals, cloned, and used to feed a culture of the above lymphocytes. Transfer of the non-mutant DNA fragment into the lymphocytes was mediated by lipofectamine, a pos. charged liposome. After the cells were fed 14 times, the repaired cells amounted roughly to 0.5% of the total tested cells.

AN 1996:295077 CAPLUS

DN 124:309568

TI Gene therapy using homologous recombination for mutation correction

IN Anvret, Maria; Blombaeck, Margareta; Zhang, Zhiping

PA Swed.

SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9604397	A1	19960215	WO 1994-SE1038	19941103
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	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9512854	A1	19960304	AU 1995-12854	19941103
PRAI	SE 1994-2642	A	19940805		
	WO 1994-SE1038	W	19941103		

L18 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

TI Construction of a functional human suppressor tRNA gene: an approach to gene therapy for β- thalassemia

AB A human tRNALysgene was converted to an amber suppressor by site-specific mutagenesis of the anticodon. The mutated tRNALysgene directed synthesis of a tRNA that suppressed the UAG amber nonsense mutation in β° thalassemia mRNA. Such genes may be used to detect other nonsense mutations in mammalian cells and may provide an approach to gene therapy for β° thalassemia due to nonsense mutations.

AN 1982:450555 CAPLUS

DN 97:50555

TI Construction of a functional human suppressor tRNA gene: an approach to gene therapy for β- thalassemia

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AU   Temple, Gary F.; Dozy, Andree M.; Roy, Kenneth L.; Kan, Yuet Wai
CS   Howard Hughes Med. Inst. Lab., Univ. California, San Francisco, CA, 94143,
     USA
SO   Nature (London, United Kingdom) (1982), 296(5857), 537-40
     CODEN: NATUAS; ISSN: 0028-0836
DT   Journal
LA   English

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            1426    FILE BIOTECHNO
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            3295    FILE CAPLUS
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           938   FILE ESBIOBASE
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